REMARKS

Applicant respectfully requests entry of the Amendment and reconsideration of the claims. Applicant currently amends claim 123 to delete an obvious typographical error of an unneeded comma. Applicant provides further remarks below and requests reconsideration and withdrawal of the objection to claim 122 and the priority and rejections under 35 U.S.C. § 102(a) and § 112, first paragraph.

Priority

The Examiner objects to the claim for the benefit of priority and contends that provisional applications 60/441,059 filed 1/16/2003, 60/488,610 filed July 18, 2003, and 60/510,314 filed October 8, 2003 do not provide support for a CDRH3-phage coat fusion protein comprising a "N terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" and a "C terminal portion of about 1 to 6 amino acids in which some or all amino acid positions are structural". The Examiner further asserts that a fusion protein comprising at least a portion of a phage coat protein is not supported in the earlier applications as well. Applicants respectfully disagree with the Examiner and request acknowledgement of the claim for priority of the currently pending claims.

1. ***N terminal and C terminal portions.*** The Examiner rejects the claim for the benefit of priority in regards to the claimed N terminal and C terminal portions as discussed above. In the response of August 20, 2008, the Examiner contends that the N terminus can be construed as anywhere before the C terminus, and the C terminus is anywhere following the protein N terminus (pages 4-5). Applicants respectfully disagree. Under the Examiner's interpretation, the central portion of the CDRH3 scaffold could qualify as both the C terminus and the N terminus. As Applicant has defined the CDRH3 scaffold in claim 105, there are 3 portions—the N terminus, the C terminus, and the central portion. Each is distinguishable. Thus, the N terminus is the start of the CDRH3 scaffold up until the central portion. The central portion of the CDRH3 scaffold, as recited in claim 105, is situated between the N terminus and the C terminus and can vary in sequence and length. The C terminus follows the central portion until the last amino acid of the CDRH3 scaffold.

In Applicant's previous response, portions of the specification were recited to provide support for the claim limitations regarding the N terminal portion and the C terminal portion of the CDRH3 scaffold. The Examiner admitted that the cited provisional applications provided support for the first four residues and the last six residues of the CDRH3. The Examiner stated that the first four residues and the last six residues do not encompass all of the N terminal portion or the C terminal portion, respectively. Applicants respectfully assert that, as discussed immediately above, the Examiner incorrectly construed the limitation of the "N terminal portion" and the "C terminal portion." Applicant respectfully asserts that claim 105 recites a CDRH3 scaffold with 3 portions—N terminus, central, and C terminus. These portions do not overlap one another as the examiner construed in his response of August 20, 2008, at pages 4-5. In view of the correct interpretation and as demonstrated by the exemplified CDRH3 scaffolds, the N terminus does not exceed 4 amino acids, and the C terminus does not exceed 6 amino acids. Thus, Applicant has fully described the N terminal portion and the C terminal portion of a CDRH3 scaffold. For at least these reasons, Applicants respectfully assert the claim of priority to the claim limitations of "N terminal portion" and "C terminal portion" of a CDRH3 scaffold.

2. ***At least a portion of a phage coat protein.*** Applicants respectfully submit that the limitation of "at least a portion of a phage coat protein" can claim priority to the '059 provisional. At page 72, line 28 to page 73, line 1, the specification describes methods for displaying fusion polypeptides comprising antibody fragments. The specification particularly cites, *inter alia*, WO 93/19172, which is expressly incorporated by reference (this section also appears in the '610 provisional at page 73, lines 21-25). WO 93/19172 discloses a fusion protein comprising an amino acid insertion after the first amino acid residue of the fd gene III mature coat protein at page 36, lines 23-34. The authors of the '172 PCT were able to display a scFv when fused to the first amino acid of the fd minor coat protein. For at least this reason, Applicant respectfully asserts that the instant application claims the benefit of priority to the '059 provisional application, filed January 16, 2003.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection to the claim to priority.

Rejection under 35 U.S.C. § 102(a)

The Examiner rejects claims 105-107, 109, 111, 113, and 115-128 under 35 U.S.C. § 102(a) as allegedly anticipated by Bond et al. (*J. Mol. Biol.*, 332:643-655 (2003)). Applicant respectfully traverses this rejection.

Applicants submit that the pending claims are entitled to a priority date of at least Jan. 16, 2003 (see argument above). The Bond et al. paper was published on September 19, 2003, and Applicant respectfully asserts that it is therefore not properly considered prior art to the instant application.

Applicant respectfully requests removal of the rejection under 35 U.S.C. § 102(a).

Rejection under 35 U.S.C. § 112, First Paragraph

The Examiner rejects claims 105-107, 109-111, and 113-128 under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner contends that the rejected limitations are new matter. Applicants respectfully traverse.

Under 35 U.S.C. §112, first paragraph, a patent specification must contain sufficient written description in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention (*Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563 (Fed. Cir. 1991)). "The specification must teach the invention by describing it." (*Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 926 (Fed. Cir. 2004)).

1. N terminal portion. The Examiner maintains the rejection for an alleged lack of written description and alleges that the limitation "an N-terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" is new matter. Applicant respectfully traverses this rejection.

Applicant respectfully asserts that the specification expressly describes the rejected claim elements. The specification at page 92, lines 11-16 recites that

> "[a] CDRH3 scaffold" comprises a N-terminal portion in which some or all of the positions are structural and a C terminal portion…In some embodiments, the N terminal portion is about 1 to 4 amino acids.

Based on at least this passage, Applicant respectfully asserts that the term "an N-terminal portion of about 1 to 4 amino acids in which some or all amino acid positions are structural" is fully described by the specification.

2. At least a portion of a phage coat protein. The Examiner rejects claim 105 (Applicant assumes that "[c]laim 1" is simply a typographical error) for reciting "at least a portion of a phage coat protein". Applicant respectfully asserts that "at least a portion of a phage coat protein" is described throughout the specification, including at page 11, lines 3-4; page 18, lines 8-9; page 55, line 28 to page 56, line 6; page 88, lines 12-13; and page 99, lines 29-31. At page 100, lines 5-15, the specification provides further description.

> [A] fusion protein comprises an antibody variable domain…fused to all or a portion of a viral coat protein. Examples of viral coat proteins include infectivity protein PIII, major coat protein PVIII, p3, Soc, Hoc, gpD (of bacteriophage lambda), minor bacteriophage coat protein 6 (pVI) (filamentous phage; J Immunol Methods. Dec. 10, 1999;231(1-2):39-51), variants of the M13 bacteriophage major coat protein (P8) (Protein Sci April 2000; 9(4):647-54). The fusion protein can be displayed on the surface of a phage and suitable phage systems include M13KO7 helper phage, M13R408, M13-VCS, and Phi X 174, pJuFo phage system (J Virol. August 2001; 75(15):7107-13.v), hyperphage (Nat Biotechnol. January 2001; 19(1):75-8). The preferred helper phage is M13KO7, and the preferred coat protein is the M13 Phage gene III coat protein.

For at least this reason, Applicant respectfully asserts that the specification fully describes "at least a portion of a phage coat protein."

3. Any hydrophobic amino acid. The Examiner rejects claim 123 and alleges that the "residue at framework position 45 may be any hydrophobic amino acid" lacks written description. Applicant respectfully traverses.

The specification supports the recitation of framework position 45 being wild-type arginine or any hydrophobic amino acid. Specifically, support for this claim can be found in Example 14 at pages 163-164 of the specification. The specification at page 163, line 31 to page 164, line 4 recites:

> Aside from Arg, both domains preferred hydrophobic residues at position 45 and the RIG domain in particular contained a substantial proportion of Trp, Phe and Leu residues. Overall, these results demonstrate that changes at positions 37 and 45 of V_HH domains relative to V_H domains contribute to protein stability, as they allow for favorable hydrophobic interactions amongst themselves and with CDR3. See Figure 52.

For at least this reason, Applicant respectfully asserts that "any hydrophobic amino acid" at framework region position 45 is fully described by the specification.

4. Another framework region. The Examiner rejects claim 126 due to the recitation of "another framework region." Applicant respectfully traverses.

Claim 123 recites "a framework region that comprises a hydrophobic amino acid at position 37 and an amino acid at position 45 selected from..." Claim 26 depends on claim 123 and recites "wherein the antibody heavy chain variable domain further comprises another framework region, wherein the another framework region comprises an amino acid at amino acid position 91..." This claim has express support in Example 7 at page 141, line 30 to page 142, line 17. Example 7 discloses a library of monobodies where four variants were generated at four framework positions—residues 37, 45, 47, and 91. These residues are the ones particularly claimed in claims 123 and 126. Residues 37, 45, and 47 are in Framework Region 2 and residue 91 is in Framework Region 3 with CDRH2 positioned between the two framework regions. Thereby, framework region 3 is the "another framework." For at least this reason, Applicant respectfully asserts that "another framework region" is fully supported by the specification.

In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejections under 5 U.S.C. § 112, first paragraph.

Rejection under Obviousness-Type Double Patenting

The Examiner provisionally rejects claims 105, 107, 109, 111, 113, 115-122 and 127-128 under the judicially created doctrine of obviousness-type double patenting over claims 22, 25, 26, 30-31, 35-37 and 48-50 of copending Application No. 11/102,502 in view of Sidhu et al. (*J. Mol. Biol.,* 296:487-495 (2000)) and evidenced by Bond et al. (*J. Mol. Biol.,* 332:643-655 (2003)). Applicant acknowledges the Examiner's rejection for obviousness-type double patenting and requests that this rejection be held in abeyance until notice of allowable subject matter.

Claim Objections

The Examiner objects to claim 122 under 37 C.F.R. § 1.75(c) as being of improper dependent form for allegedly failing to further limit the subject matter of a previous claim. Applicants respectfully traverse this rejection.

Applicant respectfully asserts claim 122 further limits claim 105. Claim 105 recites, *inter alia*, "(c) a central portion or loop of about 1 to 20 contiguous amino acids that can vary in sequence and in length." Claim 122 recites a limitation upon part (c) of claim 105. Specifically, the limitation of claim 122 requires that the central portion contain at least one variant amino acid. Claim 105 allows for a variant but does not require a variant. The central portion of the loop in (c) can contain all wild-type amino acids. Claim 122 also requires that the "at least one variant amino acid" is encoded by a non-random codon set. This is a further limitation upon the fusion protein of claim 122. For at least these reasons, claim 122 further limits the subject matter of claim 105. In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the objection to claim 122.

Summary

Applicant submits that the claims of the present application are in condition for allowance and notification to that effect is earnestly solicited. The Examiner is invited to contact Applicant's representative at the telephone number listed below, if the Examiner believes that doing so will advance prosecution.

Please charge any additional fees or credit any overpayment to Merchant & Gould P.C., Deposit Account No. 13-2725.

Respectfully submitted,

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